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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,282	08/30/2000	Maurice Kent Gately	9483	2369

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THOMAS E FRIEBEL
PENNIE & EDMONDS LLP
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
DECLOUX, AMY M	

ART UNIT	PAPER NUMBER
1644	22

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/652,282	Applicant(s) GATELY ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-20 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-20 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-7-03 has been entered.

Claims 15-20 and 37-40 are pending and under consideration.

In view of said amendment, the obvious double patenting type rejection has been withdrawn.

Drawings

The corrected or substitute drawings were received on 12-11-02. These drawings are acceptable.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-20 and 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite in the recitation of the phrase "immunologically reactive" because said phrase is not defined in the specification and the phrase has no art recognized meaning.

Response to Arguments

Applicant's arguments filed 11-9-01 have been fully considered but they are not persuasive. Applicant traverses the rejection on the grounds that the terms "immunologically" and "reacts with" have acquired a standard meaning in the art. However, the examiner notes that Applicant does not state the phrase "immunologically reactive" also has acquired a standard meaning in the art.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 15-17, 19-20, 37 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Trinchieri et al. (5,811,523), as evidenced by Gately et al. (US Patent 5,780,597, of record) and Carter et al (IDS reference 16) and Colman (Res Immunol. 1994 Jan;145(1):33-6).

The instant claims are drawn to a monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said monoclonal antibody immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit.

'523 teaches a polyclonal and monoclonal antibody which reacts with the human cytokine NKSF heterodimer (which appears to have the same sequence as IL-12 as evidenced by Gately et al.) and is specific for the 35KD subunit which has the same sequence as the sequence of the IL-12 35KD subunit, (see entire patent, especially column 10, lines 25-28, claims 1, 3-5 and 7 and Figures 1-2). Specifically, claim 1 of '523 teaches that said antibody specifically reacts with the heterodimer, and claim 3 of '523 which depends from claim 1, teaches that said antibody reacts with the p35 subunit.

'523 reads on the limitation that said antibody is not immunologically reactive with any epitope presented by said p40 subunit, because said referenced antibody, which immunologically reacts with the p35 subunit, would not immunologically react with the p40 subunit because the amino acid sequences of the two subunits are distinct and because antibody recognition is sequence dependent, as evidenced by Colman. Colman teaches that even single amino acid changes in the antigen can effectively abolish the antibody antigen interaction entirely (see entire article, including page 33, second column).

With regard to the properties of the antibodies recited in the instant claims ie the concentrations of antibody and Human IL-12 and by "inhibiting IL-12 stimulated PHA activated human lymphoblast proliferation" and "by inhibiting IL-12 stimulated IFN-γ production", the referenced antibody has the specificity of the claimed antibody, and the functional properties are

considered inherent properties of the referenced antibody. The claimed antibody appears to be the same as the referenced antibody, absent a showing of any differences. Since the Patent Office does not have the facilities for comparing the antibody of the instant invention to those of the prior art, the burden is on the applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art, see In re Best, 562 F.2d 152, 195 USPQ 430 (CCPA 1977).

With regard to the recited limitation of the antibody having cross reactivity with rheusus monkey IL-12, it is an inherent property of said recited anti-human IL-12 antibody that it would cross react with rheusus monkey IL-12 to some extent as evidenced by Carter et al who teach cross-reactivity of antibodies to IL-12 with mouse Il-12 and human IL-12 (about 60%, see especially page 367, second column, lines 6-8) and the degree of homology between human and mouse Il-12 is less than the homology between human and rhesus Il-12.

With regard to the recited limitation that the antibody is produced by a hybridoma, said production is encompassed by '523's teaching that the referenced monoclonal antibodies can be made by standard methods, which includes hybridoma technology.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 16, 18 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Trinchieri et al. (5,811,523), in view of Gately et al. (US Patent 5,780,597, of record), Carter et al (IDS reference 16), Colman (Res Immunol. 1994 Jan;145(1):33-6) and Bendig (Methods:A Companion to Methods in Enzymology Vol. 8:83-93, 1995).

Trinchieri et al. (5,811,523), Gately et al., Carter et al and Colman teach as discussed supra, but do not teach that the antibody is humanized.

Trinchieri et al. (5,811,523) further teaches that said antibodies can be used for therapeutic uses, and that NKSF (or IL-12) stimulates nk cells and IFN-γ production by PBL, (see entire patent, especially column 21, lines 14-19).

Bendig teaches that clinical results with rodent antibodies have been disappointing primarily because rodent antibodies are highly immunogenic in humans. Bendig further teaches that to help overcome this problem, rodent antibodies have been humanized, and teaches that reliable methods for humanization have been developed.

Therefore, it would have been obvious to one of skill in the art, who wanted to use the antibodies taught by '523 for in vivo therapy for humans, to have humanized the antibody taught by '523 made in rodents because Bendig teaches that the problem of immunogenicity of rodent antibodies in humans has been alleviated by humanizing rodent antibodies and because '523 teaches therapeutic uses for said antibodies directed against NKSF (IL-12). One would have an expectation of success because Bendig also teaches that reliable methods for humanization have been developed.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner
April 30, 2003

Patrick J. Nolan, Ph.D.
Primary Patent Examiner
Group 1640